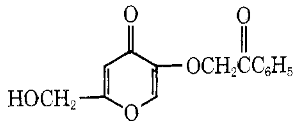
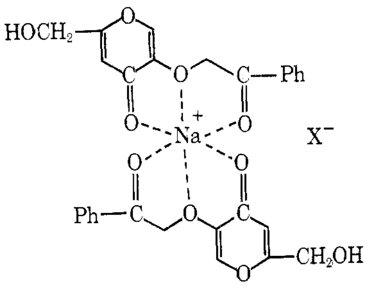
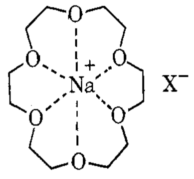
antibiotics[2] that complex with Na^+ or K^+, as monensin, nigericin, or dianemycin, which are open-chain rather than macrocyclic. Although the structures of these compounds show linear arrays of O-heterocyclic rings, the oxygens are so positioned as to surround the Na^+, thus resembling the macrocyclic esters and the crown ethers. There are but a few of the examples which have stimulated present interest.

In view of this activity, therefore, it may be helpful to those working in this field to call attention to a related but obscure observation of ours[6] which was reported in a different context 25 years ago. We observed a beautifully crystalline complex from methanol that involved 2 mol of phenacyl kojate and 1 mol of sodium halide, $2C_{14}H_{12}O_5 \cdot NaX$. The NaX was removable by treating the complex with water.

In phenacyl kojate (I) all oxygen atoms are separated by two carbon atoms, a feature which also holds for the conventional crown ethers. Structure II is proposed for the complex, by selecting OCCO sequences in phenacyl kojate that show cis relationships for the oxygens. This structure shows a striking similarity to III, the complex of a crown ether with NaX.


I


II


III

There are two important differences, however, between II and III. In the first place, all oxygens in III classify as ether oxygens whereas in II four of the six participating oxygens are from carbonyl groups and the remaining two are more properly classified as ester oxygens than ether oxygens. This suggests that many other compounds that possess properly positioned nonether oxygens may also display complexing tendencies toward Na^+, K^+, or NH_4^+. Secondly, in III a single organic molecule holds all of the oxygens, whereas in II a pair of organic molecules are involved.

Registry No.—I, 49864-67-7.

References and Notes

(1) C. J. Pedersen, *J. Amer. Chem. Soc.*, **89**, 2495, 7017 (1967); **92**, 391 (1970); H. K. Frensdorff, *ibid.*, **93**, 600, 4685 (1971); D. J. Sam and H. E. Simmons, *ibid.*, **94**, 4024 (1972); **96**, 2252 (1974); M. Svoboda, J. Hapala, and J. Zavada, *Tetrahedron Lett.*, 265 (1972); R. A. Bartsch and K. Wiegers, *ibid.*, 3819 (1972); D. J. Cram and J. M. Cram, *Science*, **183**, 803 (1974).

(2) M. R. Truter, "Structure and Bonding," Vol. 16, Springer-Verlag New York, New York, N. Y., 1973, pp 71–111.

(3) J. A. Rendleman, Jr., *J. Org. Chem.*, **31**, 1839 (1966).

(4) N. V. Sidgwick and F. Brewer, *J. Chem. Soc.*, **127**, 2379 (1925); D. Bright, G. Milburn, and M. Truter, *J. Chem. Soc. A*, 1582 (1971).

(5) B. Kilbourn, J. Dunitz, L. Pioda, and W. Simon, *J. Mol. Biol.*, **30**, 559 (1967); M. Dobler, J. Dunitz, and B. Kilbourn, *Helv. Chim. Acta*, **52**, 2573 (1973).

(6) C. D. Hurd and R. J. Sims, *J. Amer. Chem. Soc.*, **71**, 2443 (1949).

A Comparison between the Thermal and Photochemical 1,3-Cycloaddition Reactions of Ethyl 2-Methyl-3-phenylglycidate with Benzaldehyde. On the Thermal Fission of a Carbonyl Ylide

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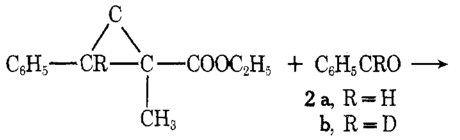
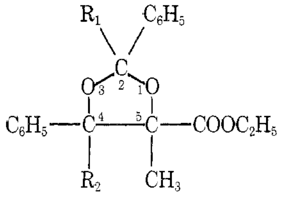
Received December 4, 1973

Compared to the wealth of information published on the photochemical behavior of oxiranes,[1] their thermochemistry has been particularly neglected. One puzzling question in this area concerns the requirements leading to the specific breaking of either the carbon–carbon or one of the carbon–oxygen bonds. In all the thermal 1,3-cycloaddition reactions of oxiranes published to date, there was cleavage of either the carbon–carbon bond[2] or one of the carbon–oxygen bonds,[3] but no competition between these two processes has been reported. This may have reflected either very different bond strengths in the oxirane or, in the case of comparable bond strengths, kinetic or thermodynamic factors in the product formation. In the cases of cycloaddition reactions with carbonyl dipolarophiles hitherto described, the products resulting from C–C or C–O bond breaking would have been chemically different and the effect of the latter factors could therefore have prevailed.

It was interesting to seek an example where *the same* structure would be obtained by either C–C or C–O bond breaking, and to use a label to determine the course of the cycloaddition reaction. We came across such a system, and recently described the photochemical cycloaddition reaction of ethyl 2-methyl-3-phenylglycidate (**1a**) with benzaldehyde (**2**) to give 2,5-diphenyl-4-methyl-4-carboethoxyl-1,3-dioxolane (**3**).[4] We proved by carbon-14 as well as by deuterium[5] labeling experiments that **2a** had added to an oxirane in which the C–C and at least one C–O bond had cleaved competitively.


1a, R = H
b, R = D

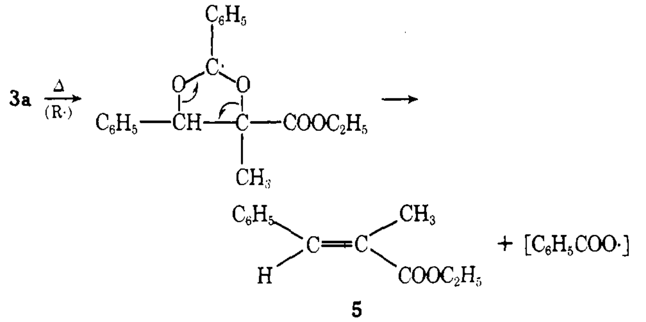
2a, R = H
b, R = D


3a, $R_1 = R_2 = H$
b, $R_1 = D$; $R_2 = H$
c, $R_1 = H$; $R_2 = D$

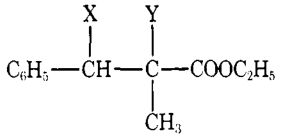
The cycloaddition of **1a** with **2a** to produce **3a** proceeded smoothly in a sealed tube at 235–280°. The treatment of **1a** with deuterated benzaldehyde (**2b**) in this temperature range yielded **3c** exclusively, the product of C–C bond cleavage in the oxirane. This was determined by nmr analysis, where the signal corresponding to H-4 was absent, and where the integration of the signal for H-2 represented a full proton. No alternate cycloaddition to **3b** followed by exchange of the acetal deuterium had taken place, since the thermal condensation of the deuterated glycidic ester **1b** and **2a** yielded **3b**, in which the signal for H-2 was absent, and where H-4 integrated for one full proton.

If we assume that, as in the photochemistry of 1,[4] the trapping of a carbon–oxygen-cleaved species by 2 would have been observed, we must conclude that within the sensitivity of the nmr technique the 1,3-cycloaddition reaction of 1 and 2 proceeds from exclusive carbon–carbon bond cleavage in the oxirane to the carbonyl ylide 4.

Extensive decomposition prevented the study of the cycloaddition reaction above 280°. When pyrolyzed alone, however, **3a** was more stable and yielded two unidentified minor products at 300° for 30 min, in addition to unreacted starting material (50%), **2a** (25%), and ethyl (*E*)-2-methylcinnamate (**5**, 25%), which was not detected in the thermolysis of **1a**. A radical participation in the thermal decomposition of 1,3-dioxolanes has been recognized,[6] and such a mechanism would account for the formation of **5**. Benzoic acid, stilbene, ethyl pyruvate, or **1a** were not detected, and the isomerization of **3a** into a benzoate such as **6** or **7**, followed by decomposition to **5**, is held to be unlikely, since the pyrolysis of benzoates to olefins is known to yield benzoic acid quantitatively.[7]

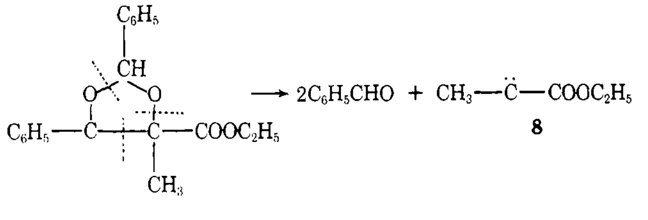


5



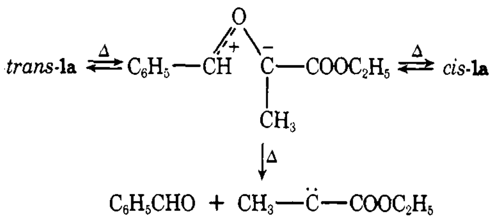
6, X = $OCOC_6H_5$; Y = H
7, X = H; Y = $OCOC_6H_5$

The fragmentation of **3a**, on the other hand, could have given two carbonyls and one carbene in three different manners. The formation of **5** by coupling of phenylcarbene and carboethoxylmethylcarbene[8] from the competition of at least two such processes is ruled out by the absence of the expected accompanying products. A cycloreversion reaction is required, however, for explaining the formation of **2a**, and the most reasonable hypothesis is for the process giving 2 mol of **2a** and 1 mol of **6**, the latter yielding polymeric products following a hydrogen shift to ethyl acrylate.

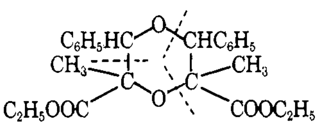


The photolysis of **1a** had yielded **3a** directly, resulting from the fission of two bonds to **2a** (with the probable formation of **8**, which we did not succeed in trapping), followed by cycloaddition of **1a** and **2a**. It is not known whether the cleavage of both bonds occurred simultaneously or not, and in this case whether or not the fission of the C–O bond preceded that of the C–C bond.

The thermolysis of **1a** at 235° also led to the direct formation of **3a** in low yield, in addition to cis–trans isomerization in the starting material. This result suggested that fission of the carbonyl ylide had occurred thermally, in contrast to Huisgen's experience with other carbonyl ylides at slightly lower temperatures.[2g] Probably each diastereoisomer of **1a** yielded a different carbonyl ylide, and these interconverted thermally, but no information on the stereochemistry of the oxirane ring opening could be deduced from these experiments.



The synthesis of 1,4-dioxanes by condensation of oxiranes or glycols is well known.[8] Consequently, the benzaldehyde required for the direct conversion of **1a** to **3a** did not necessarily come from the direct fission of the carbonyl ylide, but could have been formed by fragmentation of a dioxane such as **9**, **10**, or **11**, obtained by the dimerization of **1a** or **4**. These fragmentation reactions would also have generated at least one of the following: **5** (*E* or *Z*), ethyl pyruvate, diethyl dimethylmaleate, or diethyl dimethylfumarate. Although not visible on the nmr spectrum of the mixture obtained in the thermolysis of **1**, both diastereoisomers of **5** were detected by glc and gc–mass spectroscopy. None of the other products expected from the decomposition of **10** or **11** were observed.



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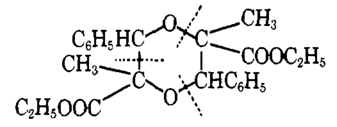
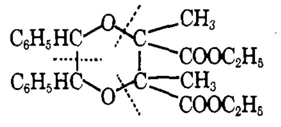


10



11

Ethyl pyruvate was not stable under the conditions of the thermolysis, as shown by a control experiment in which a mixture with **1a** was pyrolyzed for 2 hr at 275°. Consequently, it is not possible at this time to tell whether **5** originated with the decomposition of **3** or with that of **9**, and whether or not the thermolysis of **1** produced **2** by fission of a carbonyl ylide remains to be determined.

Experimental Section

Ethyl 2-Methyl-3-deuterio-3-phenylglycidate (1b). A sodium ethoxide solution (from 1.1 g of Na in 50 ml of absolute EtOH) was added over 1.5 hr under N_2 to a solution of 5 g of **2b** and 8.5 g of ethyl 2-bromopropionate in 10 ml of absolute EtOH with stirring in an ice bath. After stirring for 1 hr, 100 ml of H_2O was added and the solution was extracted with three 30-ml portions of ether which were combined, dried over $MgSO_4$, and evaporated. The yellow residue was distilled and yielded 4.1 g of **1b**: bp 120–125° (3 Torr); nmr ($CDCl_3$) cis isomer at 0.9 (t, J = 7 Hz, 3 H), 1.77 (s, 3 H), 3.9 (q, J = 7 Hz, 2 H), and 7.28 ppm (s, 5 H), trans isomer at 1.3 (s, 3 H), 1.3 (t, J = 7 Hz, 3 H), 4.25 (q, J = 7 Hz, 2 H), and 7.28 ppm (s, 5 H).

Ethyl *trans*-2-Methyl-3-phenylglycidate (*trans*-1a). *trans*-α-Methylcinnamic acid (10.0 g) was treated with EtOH and H_2SO_4 at reflux and yielded 9.2 g of ester: nmr ($CDCl_3$) 1.25 (d, J = 7.5 Hz, 3 H), 2.05 (d, J = 1.5 Hz, 3 H), 4.15 (d, J = 7.5 Hz, 2 H), 7.23 (s, 5 H), and 7.6 ppm (q, J = 1.5 Hz, 1 H). This was epoxidized with *m*-chloroperoxybenzoic acid in $CHCl_3$ at reflux for 16 hr. After work-up, there was obtained 6.5 g of *trans*-**1a**: bp 121–123° (3 Torr); nmr ($CDCl_3$) 1.26 (s, 3 H), 1.29 (t, J = 7 Hz, 3 H), 4.20 (q, J = 7 Hz, 2 H), 4.29 (s, 1 H), and 7.27 ppm (s, 5 H).

Ethyl *cis*-2-Methyl-3-phenylglycidate (*cis*-1a). A mixture of glycidic esters from the Darzens reaction which contained 53% of the cis isomer was saponified with 0.5 equiv of KOH in absolute EtOH with stirring at room temperature for 3 min. After filtration of the pure trans salt, the solution was diluted with water and extracted with ether. The extract was dried, concentrated, and distilled at 97–99° (0.5 Torr) to yield 6 g of a mixture which was 94% *cis*- and 6% *trans*-1a. Pure *cis*-1a may be obtained by using 1.1 equiv of base with respect to the trans ester in the mixture.

Thermolysis of 1a. General Procedure. The Pyrex tubes were thoroughly washed with 6 *N* NaOH, water, and acetone and flame dried. After either the ester **1a** or an equimolar mixture of **1** and **2** was introduced, the tube was sealed and placed in a sand bath. Identical results were obtained when soft glass washed as described above was used instead of Pyrex, or when the tubes were washed with concentrated HCl, water, and acetone and flame dried. Just before use, **2** was washed with aqueous $NaHCO_3$ and distilled from Zn dust. The sample of **2b** was prepared according to Burgstahler, *et al.*,[9] and was pure from nmr.

A. A 250-mg sample of *trans*-**1a** was heated at 230° for 17 hr. Over 90% of the starting material was still present, but as a mixture of 84% trans and 16% cis isomers. Some **2a** and **3a** were also identified by glc and nmr.

B. A 250-mg sample of **1a** containing 94% of the cis isomer was heated for 3.5 hr at 270°. Over 90% of **1a** containing 60% of the trans isomer was recovered, in addition to small amounts of **2a, 3a,** and **5.**

C. A mixture of **1a** (200 mg, *ca.* 50% trans) and **2a** (100 mg) produced 16% conversion to **3a** when heated at 235° for 2 hr, and 60% conversion to **3a** when heated at 280° for 2 hr. However, decomposition took place, and no **3a** could be isolated above 300°. The isomer of **3a** obtained in these experiments was the same as that obtained photochemically, with nmr (CCl_4) at 0.90 (t, $J = 7$ Hz, 3 H), 1.75 (s, 3 H), 3.65 (q, $J = 7$ Hz, 2 H), 4.95 (s, 1 H), 6.00 (s, 1 H), and 7.25–7.90 ppm (10 H).[10] The sample of **3c** obtained by thermolysis of **1a** and **2b** was identical, except for the absence of the 4.95-ppm signal, while the signal at 6.00 was missing in **3b** from the thermolysis of **1b** and **2a.**

Thermal Stability of Ethyl Pyruvate. A mixture of 0.169 of ethyl pyruvate and 0.200 g of **1a** (60% cis) was heated as above for 2 hr at 275°. Nmr and gc–mass spectra showed that no ethyl pyruvate was present in this reaction mixture.

Thermolysis of 3a. A crystalline sample of **3a** did not show any change when heated in a sealed tube at 250° for 2 hr. After 0.5 hr at 300°, the nmr integration showed 50% **3a,** 25% **2a,** and 25% ethyl (*E*)-α-methylcinnamate. The assignments were confirmed by glc and glc–mass spectra against authentic samples. Neither **1a** nor benzoic acid was detected.

Acknowledgment. We are indebted to the National Science Foundation for its opinion that "a study of the thermal reactions of oxiranes could have no practical applications since most laboratories are not equipped for performing reactions at the temperatures herein reported, and it will not provide answers to problems that people are interested in."

Registry No.—*cis*-**1a**, 7042-28-6; *trans*-**1a**, 7141-24-4; *cis*-**1b**, 52123-63-4; *trans*-**1b**, 52123-64-5; **2a**, 100-52-7; **2b**, 3592-47-0; **3a**, 40707-69-5; ethyl 2-bromopropionate, 535-11-5; *trans*-α-methylcinnamic acid, 1895-97-2.

References and Notes

(1) G. W. Griffin, *Angew. Chem., Int. Ed. Engl.*, **10**, 537 (1971).
(2) (a) W. J. Linn and R. E. Benson, *J. Amer. Chem. Soc.*, **87**, 3657 (1965); (b) W. J. Linn, *ibid.*, **87**, 3665 (1965); (c) W. J. Linn and E. Ciganek, *J. Org. Chem.*, **34**, 2146 (1969); (d) A. Robert, J. J. Pommeret, and A. Foucaud, *Tetrahedron Lett.*, 231 (1971); (e) A. Robert, J. J. Pommeret, E. Marchand, and A. Foucaud, *Tetrahedron*, **29**, 463 (1973); (f) H. Hamberger and R. Huisgen, *Chem. Commun.*, 1190 (1971); (g) A. Dahmen, H. Hamberger, R. Huisgen, and V. Markowski, *ibid.*, 1192 (1971).
(3) H. H. Wasserman and E. H. Barber, *J. Amer. Chem. Soc.*, **91**, 3674 (1969); W. K. Anderson and T. Veysoglu, *J. Org. Chem.*, **38**, 2267 (1973).
(4) J. Kagan, J. T. Przybytek, B. E. Firth, and S. P. Singh, *Tetrahedron Lett.*, 5133 (1972).
(5) J. Kagan, B. E. Firth, and J. T. Przybytek, unpublished results.
(6) W. B. Guenther and W. D. Walters, *J. Amer. Chem. Soc.*, **73**, 2127 (1951).
(7) C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960).
(8) These reactions are usually acid catalyzed: C. B. Kremer and L. K. Rochen in "Heterocyclic Compounds," Vol. 6, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1957, p 1. However, thermal syntheses may also take place: E. J. Jahn and H. Hibbert, *Can. J. Res.*, **8**, 199 (1933).
(9) A. W. Burgstahler, D. E. Walker, Jr., J. P. Kuebrich, and R. L. Schowen, *J. Org. Chem.*, **37**, 1272 (1972).
(10) The chemical shifts reported for **3a** in ref 4 were in error.

On the Perlactone *vs.* Dioxetanol Intermediates in the Thermal and Base-Catalyzed Autoxidation of Ethyl 2-Oxo-3-phenylbutyrate

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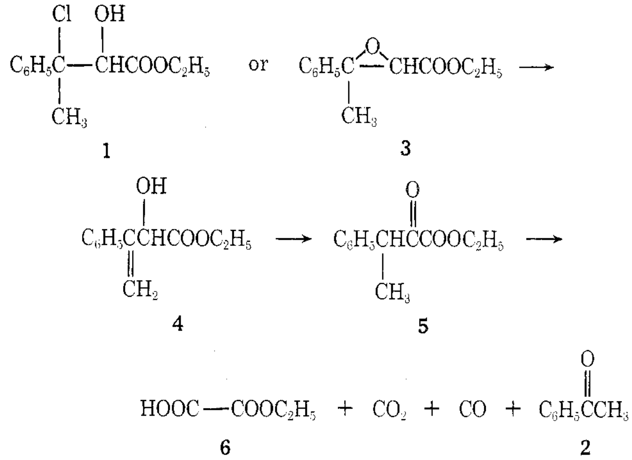
As part of a study on the mechanism of the migration of an ethoxycarbonyl group to an electron-deficient center,[1] the dehydrochlorination of ethyl 2-hydroxy-3-chloro-3-phenylbutyrate (**1**) at 132° was investigated. Surprisingly, acetophenone (**2**) was a major product.

The shortest pathway from **1** to **2** involved the epoxide **3** obtained by dehydrochlorination, in which an oxygen atom was at the required position. While **3** was found to be converted into **2** under the acidic reaction conditions, nmr showed that both **1** and **3** initially yielded the allylic alcohol **4**, which further isomerized into the keto ester **5** in the presence of an excess of acid. This product was the actual precursor to **2**, and also yielded carbon monoxide, carbon dioxide, ethanol, and monoethyl oxalate at 132°. The conversion was accelerated by bubbling air through the solution, and was completely suppressed in the absence of oxygen. There was no oxidation with singlet oxygen, generated photochemically with rose Bengal as sensitizer, or obtained from the triphenyl phosphite–ozonide adduct.



$$\mathrm{C_6H_5}\underset{\mathrm{CH_3}}{\overset{\mathrm{Cl}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\mathrm{C}}\mathrm{HCOOC_2H_5}\ \text{or}\ \mathrm{C_6H_5}\underset{\mathrm{CH_3}}{\mathrm{C}}\overset{\mathrm{O}}{\frown}\mathrm{CHCOOC_2H_5} \longrightarrow$$

1 3

$$\mathrm{C_6H_5}\underset{\mathrm{CH_2}}{\overset{\mathrm{OH}}{\mathrm{C}}}\mathrm{CHCOOC_2H_5} \longrightarrow \mathrm{C_6H_5}\underset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{H}\overset{\mathrm{O}}{\mathrm{C}}\mathrm{COOC_2H_5} \longrightarrow$$

4 5

$$\mathrm{HOOC{-}COOC_2H_5} + \mathrm{CO_2} + \mathrm{CO} + \mathrm{C_6H_5}\overset{\mathrm{O}}{\mathrm{C}}\mathrm{CH_3}$$

6 2

A mechanism patterned after the well-known cumene oxidation to phenol and acetone was considered, in which a hydroperoxide is decomposed with acid, and undergoes a phenyl migration from carbon to oxygen.[2] The corresponding rearrangement in **7** with either phenyl or methyl migration could not possibly give **2**, and needs no further consideration.

The migration of the acyl moiety from carbon to oxygen[3] in the decomposition of **7** would produce a tertiary, oxygen-stabilized, benzylic cation intermediate **8.**

Subsequent decomposition as shown in Scheme I, incorporating the molecule of water produced in the conversion of **7** to **8**, would account for the observed products. For the sake of convenience, this decomposition is written as pro-